Homocystinuria

Description

Homocystinuria is an inherited disorder in which the body is unable to process certain building blocks of proteins (amino acids) properly. There are multiple forms of homocystinuria, which are distinguished by their signs and symptoms and genetic cause. The most common form of homocystinuria is characterized by nearsightedness (myopia), dislocation of the lens at the front of the eye, an increased risk of abnormal blood clotting, and brittle bones that are prone to fracture (osteoporosis) or other skeletal abnormalities. Some affected individuals also have developmental delay and learning problems.

Less common forms of homocystinuria can cause intellectual disability, failure to grow and gain weight at the expected rate (failure to thrive), seizures, problems with movement, and a blood disorder called megaloblastic anemia. Megaloblastic anemia occurs when a person has a low number of red blood cells (anemia), and the remaining red blood cells are larger than normal (megaloblastic).

The signs and symptoms of homocystinuria typically develop within the first year of life, although some mildly affected people may not develop features until later in childhood or adulthood.

Frequency

The most common form of homocystinuria affects at least 1 in 200,000 to 335,000 people worldwide. The disorder appears to be more common in some countries, such as Ireland (1 in 65,000), Germany (1 in 17,800), Norway (1 in 6,400), and Qatar (1 in 1, 800). The rarer forms of homocystinuria each have a small number of cases reported in the scientific literature.

Causes

Mutations in the *CBS*, *MTHFR*, *MTR*, *MTRR*, and *MMADHC* genes cause homocystinuria.

Mutations in the *CBS* gene cause the most common form of homocystinuria. The *CBS* gene provides instructions for producing an enzyme called cystathionine beta-synthase. This enzyme acts in a chemical pathway and is responsible for converting the amino acid homocysteine to a molecule called cystathionine. As a result of this pathway, other

amino acids, including methionine, are produced. Mutations in the *CBS* gene disrupt the function of cystathionine beta-synthase, preventing homocysteine from being used properly. As a result, this amino acid and toxic byproducts substances build up in the blood. Some of the excess homocysteine is excreted in urine.

Rarely, homocystinuria can be caused by mutations in several other genes. The enzymes made by the *MTHFR*, *MTR*, *MTRR*, and *MMADHC* genes play roles in converting homocysteine to methionine. Mutations in any of these genes prevent the enzymes from functioning properly, which leads to a buildup of homocysteine in the body. Researchers have not determined how excess homocysteine and related compounds lead to the signs and symptoms of homocystinuria.

Learn more about the genes associated with Homocystinuria

- CBS
- MMADHC
- MTHFR
- MTR
- MTRR

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. Most often, the parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs and symptoms of the condition.

Although people who carry one mutated copy and one normal copy of the *CBS* gene do not have homocystinuria, they are more likely than people without a *CBS* mutation to have shortages (deficiencies) of vitamin B12 and folic acid.

Other Names for This Condition

- Cystathionine beta synthase deficiency
- Homocysteinemia

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Classic homocystinuria (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0751202/)
- Genetic Testing Registry: Homocystinuria (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0019880/)

- Genetic Testing Registry: Homocystinuria due to methylene tetrahydrofolate reductase deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1856058/)
- Genetic Testing Registry: Homocystinuria, cblD type, variant 1 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1848553/)

Genetic and Rare Diseases Information Center

- Homocystinuria (https://rarediseases.info.nih.gov/diseases/10770/homocystinuria)

Patient Support and Advocacy Resources

- Disease InfoSearch (https://www.diseaseinfosearch.org/)
- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov (https://clinicaltrials.gov/ct2/results?cond=%22homocystinuria%22)

Catalog of Genes and Diseases from OMIM

- HOMOCYSTINURIA DUE TO CYSTATHIONINE BETA-SYNTHASE DEFICIENCY (https://omim.org/entry/236200)
- HOMOCYSTINURIA DUE TO DEFICIENCY OF N(5,10)-METHYLENETETRAHYDROFOLATE REDUCTASE ACTIVITY (https://omim.org/entry/236250)
- HOMOCYSTINURIA-MEGALOBLASTIC ANEMIA, cblE COMPLEMENTATION TYPE (https://omim.org/entry/236270)
- HOMOCYSTINURIA-MEGALOBLASTIC ANEMIA, cblG COMPLEMENTATION TYPE (https://omim.org/entry/250940)
- METHYLMALONIC ACIDURIA AND HOMOCYSTINURIA, cblD TYPE (https://omim.org/entry/277410)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Homocystinuria%5BMAJR%5D%29+AND+%28homocystinuria%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D)

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